

**What is claimed is:**

1. An electrospray ionization (ESI) device for mass spectrometric analysis comprising:  
a fluidic chip formed with an electrospray emitter fluidly connected to a calibration  
solution that produces an expected ESI signal in a mass spectrometer;  
5 an input/output (I/O) controller that is coupled to an electrospray assembly  
including at least one of the following: an XYZ stage to position the electrospray emitter  
relative to a mass spectrometer orifice; a power supply connected to the fluidic chip for  
applying an adjustable electrospray ionization voltage; and an adjustable flow regulator  
connected to the fluidic chip for regulating flow of the calibration solution; and  
10 a central processing unit coupled to a memory having an optimization algorithm for  
optimizing electrospray conditions of the calibration solution by instructing the I/O  
controller to selectively control the electrospray assembly based on resultant signals from  
the mass spectrometer to achieve the expected ESI signal for the calibration solution.
- 15 2. The ESI fluidic device as recited in claim 1, wherein the ESI fluidic chip is a  
microfluidic chip.
3. The ESI fluidic device as recited in claim 1, wherein the power supply is also  
connected to the mass spectrometer orifice.

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4. A method of obtaining optimal electrospray ionization (ESI) conditions comprising the following steps of:

selecting an automated ESI optimization assembly for controlling an electrospray ionization interface that includes a microfluidic device and a mass spectrometer for

5 measuring expected ESI signals for the calibration standard;

selecting a set of initial spray conditions including an initial position, an ESI voltage and a flow rate for the calibration standard;

applying the set of initial spray conditions to the electrospray ionization interface using the ESI optimization assembly to generate resulting ESI signals for the calibration

10 standard in the mass spectrometer;

measuring the resulting ESI signals for the calibration standard in the mass spectrometer; and

adjusting at least one initial spray condition with the automated ESI optimization assembly until the expected or optimal ESI signals for the calibration standard are obtained.

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5. The method as recited in claim 4, wherein the expected ESI signals are observed and characterized by at least one of the following: a substantially constant electrospray current, a relatively stable Taylor cone formation, a relatively high, stable detected ion signal for the calibration standard(s), and a relatively high, stable current at selected

20 locations within the mass spectrometer.

6. The method as recited in claim 4, wherein at least one of the initial spray conditions is adjusted according to an automated feedback loop based on the resulting ESI signals for the calibration standard in the mass spectrometer.

5 7. The method as recited in claim 4, wherein the ESI optimization assembly includes a controller to control positioning of an XYZ stage on which the microfluidic device is mounted.

8. The method as recited in claim 4, wherein the ESI optimization assembly includes a  
10 controller to control delivery of power to a voltage source that generates the ESI voltage.

9. The method as recited in claim 4, wherein the ESI optimization assembly includes a controller to control flow from a fluid source that delivers the calibration standard.

15 10. The method as recited in claim 7, wherein the microfluidic device mounted on the XYZ stage is moved to a desired location relative to the entrance of a mass spectrometer that is derived from prior experimentation.

11. The method as recited in claim 10, wherein the XYZ stage includes at least one of  
20 the following: a single-dimension translation; a two-dimension translation; and a three-dimension translation.

12. A method for optimizing an electrospray ionization (ESI) process comprising the following steps of:

selecting a microfluidic device formed with an electrospray tip, wherein the microfluidic device includes: at least one analyte reservoir for supplying to the electrospray tip an analyte solution through a first channel formed in the device; and a calibrant reservoir for supplying to the electrospray tip a calibrant that generates an optimal value for a selected ESI parameter through a second channel formed in the device;

positioning the electrospray tip relative to an orifice in the mass spectrometer;

introducing an electrospray of the calibrant into the orifice of the mass spectrometer

10 by implementing an initial set of electrospray interface conditions;

measuring the selected ESI parameter resulting from implementation of the initial set of electrospray interface conditions; and

automatically adjusting at least one of the electrospray interface conditions using an automated ESI optimization assembly to obtain the optimal value for the selected ESI

15 parameter.

13. The method as recited in claim 12, wherein the selected ESI parameter is an expected ESI signal in the mass spectrometer for the calibrant.

20 14. The method as recited in claim 12, wherein the selected ESI parameter is an expected ESI current for the calibrant.

15. The method as recited in claim 12, wherein the optimal value for the selected ESI parameter falls within a range of preferred values.

16. The method as recited in claim 12 further comprising the step of:

5 introducing an electrospray of the analyte solution into the orifice of the mass spectrometer to generate a mass spectrum or spectra for the analyte solution.

17. The method as recited in claim 16, wherein the first channel and the second channel are non-converging channels.

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18. The method as recited in claim 16, wherein the first channel and the second channel are converging channels that permit mixing of the analyte solution from the first channel and the calibrant from the second channel.

15 19. The method as recited in claim 18, wherein the first channel and the second channel converge with a third channel which leads to the electrospray tip.

20. The method as recited in claim 19, wherein the electrospray of the calibrant is introduced into the mass spectrometer orifice before the electrospray of the analyte solution is introduced into the mass spectrometer orifice.

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21. The method as recited in claim 16, wherein the electrospray of the calibrant is introduced into the mass spectrometer orifice before the electrospray of the analyte solution is introduced into the mass spectrometer orifice.

5 22. The method as recited in claim 18, wherein the first channel and the second channel converge at the electrospray tip.

23. The method as recited in claim 16, wherein the electrospray of the calibrant is introduced into the mass spectrometer orifice simultaneously as a co-mixture with the  
10 analyte solution.

24. The method as recited in claim 16, wherein the selected ESI parameter is an optimal ESI signal for the calibrant that is measured simultaneously with the analyte solution.